view. Navigation software is also progressing; luminal "fly through" navigation can be automated and collision avoidance techniques used, with simultaneous antegrade and retrograde viewing.

At present, full colonic cleansing is mandatory for an acceptable examination, but workers are already investigating the possibility of using oral contrast medium with a view to tagging faecal residue so that it can be differentiated from pathological features and possibly digitally excluded from the image. Furthermore, because virtual colonoscopy generates images of the colonic wall, it is possible to apply algorithms that automatically detect and label regions where it is thickened, alerting the radiologist to the possible presence of polyps. Perhaps flat adenomas can be detected this way.

The development and refinement of all of these techniques are likely to have tremendous impact on the speed and accuracy of virtual colonoscopy and its interpretation in the near future. The performance characteristics of virtual colonoscopy are certain to improve with improvements in hardware and software innovation and radiologists' experience. With regard to its potential as a screening tool, its performance in real populations and its cost, patient acceptability, and availability will need to be determined.

Competing interests: None declared.

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Lesson of the week

Oestrogen and calcium homeostasis in women with hypoparathyroidism

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Oestrogen status can affect the requirement for vitamin D in women with hypoparathyroidism

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Permanent hypoparathyroidism occurs in 0.2%-0.3% of patients who undergo thyroid surgery [1]; it arises less frequently as an inherited or as an autoimmune disease. The condition is treated with vitamin D analogue drugs, doses of which have to be titrated against the serum calcium concentration while avoiding hypercalciuria. The vitamin D requirements in women with hypoparathyroidism can change if their oestrogen status alters. An awareness of this can avoid hypercalcaemia.

Case reports

Case 1

A 54 year old woman had undergone thyroidectomy for Graves' disease 34 years previously and had been treated with vitamin D since that time. She had remained euthyroid, and her serum calcium concentration had been satisfactory and stable for several years on 1α-hydroxycholecalciferol treatment (1 μg/day). The patient's parathyroid hormone concentration was below the level of detection, although her calcitonin concentration was measurable (32 ng/l, reference range < 45 ng/l). Two months after stopping hormone replacement therapy she developed symptoms of hypercalcaemia—anorexia, nausea, abdominal pain, constipation, and weight loss of 9 kg. Hypercalcaemia was confirmed biochemically; her calcium concentration, adjusted for albumin, was 3.5 mmol/l. Her dose of 1-α-hydroxycholecalciferol, calcium intake, and compliance with treatment were unchanged. She had been on hormone replacement therapy for 8 years—a cyclical regimen had been prescribed initially, and thereafter a continuous combined preparation. After 1-α-hydroxycholecalciferol was stopped, her calcium concentration returned to normal. Her serum calcium concentration subsequently remained within the reference range on a reduced dose of 1-α-hydroxycholecalciferol (0.25 μg/day).

Case 2

A 52 year old woman with idiopathic hypoparathyroidism had been treated for 30 years with vitamin D analogues. For many years she had been taking 1α-hydroxycholecalciferol (3 μg/day). At annual review she was hypercalcaemic (calcium concentration adjusted for albumin, 3.1 mmol/l) and had anorexia, nausea, and weight loss of 12 kg. Before this her serum calcium concentration had consistently been within the reference range. There had been no change in her

calcium intake or in compliance with treatment. Her calcium concentration returned to normal values after the dosage of 1›Æhydroxycholecalciferol was reduced to 1 g on alternate days. Further inquiry showed that her last menstrual period had been 3 months before the discovery of hypercalcaemia, and her postmeno› pausal status was confirmed by the finding of raised gonadotrophin concentrations (follicle stimulating hormone 93 U/l, luteinising hormone 109 U/l).

Case 3

A 51 year old woman had been treated with vitamin D analogues and thyroxine supplements for 13 years since developing persistent hypoparathyroidism and hypothyroidism after subtotal thyroidectomy for Graves' disease. Her serum calcium concentrations had been within the reference range until October 1988, when she presented with a 6 month history of weight loss of 9 kg, nausea, vomiting, thirst, and intermittent confusion. She was also menopausal. There had been no change in her dose of 1› Æhydroxycholecalciferol (2 g/day), calcium intake, or compliance with treatment. Hypercalcaemia was confirmed (the calcium concen› tration, adjusted for albumin, was 3.25 mmol/l). Her calcium concentration returned to normal and her symptoms resolved after intravenous rehydration treatment and an interval without vitamin D therapy. Treatment with 1› Æhydroxycholecalciferol was reintro› duced at a reduced daily dose of 0.25 g, and the patient's calcium concentrations remained within the reference range thereafter.

Comment

These three cases show that a change in oestrogen status can alter sensitivity to a potent vitamin D analogue in women who do not have the ability to produce parathyroid hormone. In a similar case, reported in 1979, a patient became hypercalcaemic after stopping the oral contraceptive pill.[2 3] Reintroduction of oestro› gen was associated with a fall in her serum calcium con› centration. The anti›oestrogenic activity of danazol — prescribed for endometriosis in a patient with idiopathic hypoparathyroidism who was being treated with 1› Æ hydroxycholecalciferol — resulted in hypercalcaemia and a reduced maintenance requirement for 1› Æhydroxyc› holecalciferol.[4] Hypercalcaemia can also occur immedi› ately after delivery in women with hypoparathyroidism treated with vitamin D supplements.[5 6] All these observations support a crucial role for oestrogen in cal› cium regulation in these women.

Oestrogen, 1,25›dihydroxyvitamin D, and parathy› roid hormone influence bone metabolism. Cytokines are now recognised as pivotal mediators of oestrogen, which acts on oestrogen receptors on osteoblasts[7] and osteoclasts[8] to inhibit bone resorption.[9] In normal women, oestrogen withdrawal increases bone resorp› tion and causes a rise in serum calcium. 1,25› dihydroxyvitamin D is now known to be the major direct regulator of active transcellular calcium absorp› tion via vitamin D receptors in intestinal mucosal cells.[10] Oestrogen can increase calcium absorption directly and indirectly by stimulating 1› Æhydroxylase activity in the kidney.[11] Withdrawal of oestrogens would theoretically reduce calcium absorption, and hypercal› caemia in these cases cannot be explained by this mechanism. Ultimately, the effects of oestrogen on bone and calcium metabolism are monitored by the calcium sensing receptor on parathyroid cells,[12] which respond by altering parathyroid hormone secretion. Parathyroid hormone is a major modulator of osteoclast activity. In the absence of parathyroid hormone, the positive effect on osteoclast activity and bone resorption of withdrawal of oestrogen becomes much more important for calcium regulation. In the absence of parathyroid hormone, the balance between the action of 1,25›dihydroxyvitamin D, which is a potent inducer of bone resorption,[13] and of oestrogen, which inhibits bone resorption, may become more crucial. A clinical awareness of this phenomenon allows appropriate monitoring of patients and adjustment of their dose of vitamin D at the menopause or while starting or stopping hormone replacement therapy.

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Corrections and clarifications

Screening of newborn infants for cholestatic hepatobiliary disease with tandem mass spectrometry
In this paper by I Mushtaq et al (21 August, pp 471›7) the x axis in figure 3 should have been labelled 1›specificity.

Minerva
Minerva has made a mistake—the fourth paragraph in the issue of 2 October reports a trial of cognitive behaviour therapy in depression. It was published in Archives of General Psychiatry 1999;56:829›35 (not the British Journal of Psychiatry).

Letters
In the letter by Philip C Herbert (26 June, p 1762), a wrong currency conversion was given. $C40 000 is equivalent to about £16 300 [not £92 000].